REMARKS/ARGUMENTS

Claims 1-28 are currently pending in the present application. Claims 3, 4, and 16-27 are withdrawn in response to the restriction requirement. Claim 1 is the independent claim, which is drawn to a method of detecting B. anthracis by measuring binding interactions between *Bacillus anthracis* protective antigen and an added antibody via competitive fluorescence polarization. Claims 6-15 depend from claim 1 and add further limitations. Claims 2, 5 and 28 are canceled.

I. Claims Objections

Claims 1, 6 and 28 are objected to because of they contain non-elected subject maters which must be removed from the claim. As a basis for this objection, the Office Action states:

Claim 1 has non-elected species fluorescence lifetime or fluorescence resonance energy transfer.

Claim 6 contains non-elected protein fragments.

Claim 28 contains non-elected protein species.

Response

The Applicants hereby amend Claims 1, 6 and 28 as follows:

Claim 1 is amended to delete the non-elected species "fluorescence lifetime or fluorescence resonance energy transfer".

Claim 6 is amended to delete the phrase "protein or fragments of said protein" and add the phrase "polypeptide."

Claim 28 is canceled so only *B. anthracis* protective antigen is used for this method.

As amended, informalities of claims 1, 6, and 28 are corrected. The Applicants respectfully request that the objections against these claims be withdrawn.

II. Claims Rejections – 35 USC § 112, second paragraph

Claims 1, 2, 5-15 and 28 are rejected under 35 USC §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as invention. As a basis for this rejection, the Office Action states:

Claim 1 is vague and confusing because i) it is unclear what is being mixed together in step (a); and ii) it is unclear which binding interaction is being detected in step (c). Claim 1 is incomplete because i) there is no correlation step between the detection of binding interaction in part (c) of claim 1 and estimating the concentration in a sample of a B. anthracis bacterium in the preamble; and ii) there is no control step in the method, which is an essential step of Fluorescence Polarization.

Claim 2 is vague and indefinite because it is unclear what change is being detected and what the specific change indicates about the concentration of B. anthracis in a sample.

Claim 5 is vague and confusing because it is unclear how the assay would function properly without both a positive and a negative control solution.

Claim 7 is vague and confusing because there is unclear how protein detection correlates to the estimation of B. anthracis bacterium. Additionally, it appears a binding interaction is being detected, not a specific concentration of protein in claim 1.

Claim 9 and 10 are vague and indefinite because it is unclear what is meant by a 'concentrated' or 'unconcentrated' sample.

Claim 13 is vague and confusing because there is no reference to 'sample minipolarization' in claim 1 from which it depends.

Claim 15 is vague and indefinite because it is unclear what is encompassed by "other clinical and laboratory specimens and samples'.

Response

By this amendment, claims 1, 7, 13 and 15 are amended and claims 2 and 5 are cancelled, thus obviating the rejection.

The preamble of claim 1 is amended to recite "a competitive method for detecting *Bacillus anthracis* in a sample" and thus providing the correlation between the detection of binding interaction in step (d) and the preamble. Claim 1 is also amended to incorporate the limitations of claim 2 and 5 into claim 1 to i) provide positive and negative controls, and ii) to show that detection of binding interaction between antigen in the sample and the antibody is accomplished via comparing fluorescent polarization readings between the mixture and the negative control and positive control solutions. Applicants hereby cancel claims 2 and 5.

Claim 6 has been amended to recite "*Bacillus anthracis* polypeptide" to agree with claim 1.

Claim 1 and dependent Claim 7 have been amended to recite "detecting *Bacillus anthracis*" instead of "estimating the concentration in a sample of a *Bacillus anthracis*".

Claims 9 and 10 have been amended to recite "samples suspected of containing high concentration of said *Bacillus anthracis* protective antigen" and "suspected of containing low concentration of said *Bacillus anthracis* protective antigen". Support for this amendment can be found in pages 3-4, paragraphs 26 and 30 of the published application (US 2004/0235075 A1).

Claim 13 is amended to recite "measured fluorescence polarization of said mixture" instead of "millipolarization". Its antecedent basis can be found in claim 1, step (d).

Claim 15 is amended to delete "other clinical and laboratory specimens and samples'.

As amended, Applicants respectfully request the rejection of claim 1, 7, 13, and 15 based on 35 USC § 112, second paragraph be reconsidered and withdrawn.

III. Claims Rejections – 35 USC § 112, first paragraph

Claims 1, 2, and 5-15 are rejected under 35 USC §112, first paragraph, because the specification while being enabling for fluorescence polarization assays which use protective antigen from B. anthracis for the detection of B. anthracis, does not reasonably provide enablement for methods which use any polypeptide from B. anthracis for detecting B. anthracis.

Response

Applicants hereby amend claim 1 by changing its preamble from "estimating the concentration in a sample of a" to "detecting *Bacillus anthracis* in a sample". Thus, the recited detection method is only directed to a fluorescence polarization assay for detection of *B. anthracis* in a sample using *B. anthracis* protective antigen. Applicants respectfully request the rejections based on 35 USC §112, first paragraph be reconsidered and withdrawn.

IV. Claims Rejection – 35 USC §103(a)

Claims 1, 2, 5-15 and 28 are rejected under 35 USC 103(a) as being unpatentable over Tencza et al (J. Clin. Microbiol. May 2000. 38(5): 1854-1859) and Nielson et al (J. Immunolg. Methods. 1996. 195: 161-168) in view of Simonson et al (US 6, 927, 068 B2).

Tencza et al teach the development of a fluorescence polarization-based diagnostic assay for equine infectious anemia virus (EIAV). Tencza uses FP as a tool to monitor protein-protein, protein-

peptide, and other intermolecular reactions in a sample and detect the presence of EIAV-specific antibodies in a sample. Tencza et al also teach that negative and positive controls are used in the FP assay. However, Tencza fails to teach a competitive method, which detects a specific antigen in the sample. More specifically, Tencza does not teach the addition of an antigen specific antibody to the sample as recited in amended claim 1, step (a). Furthermore, Tencza fails to teach protective antigen as a target of diagnostic assay for *B. Anthracis*.

Nielsen et al teach a homogenous fluorescence polarization assay for detection of antibody to Brucella abortus. A fluorescein labeled B. abortu O-polysaccharide tracer and a negative control were used in the assay. Nielsen indicates that the possibility of adapting the test to detect exposure to other pathogens. Similar to Tencza, Nielsen fails to teach the detection of a target antigen in the sample and does not require an addition of an antigen-specific antibody to the sample. Nielsen also fails to teach protective antigen as a prominent antigen of *B. anthracis*, which can be used in diagnostic assays.

Simonson teaches a rapid and non-invasive method to detect the presence of protective antigen from B. anthracis, which includes mixing a body fluid sample suspected of exposure of B. anthracis with a labeled B. anthracis polypeptide. The body fluid samples disclosed in Simonson include: saliva, oral rinse expectorant, oral fluid including oral mucosal transudate and gingival crevicular fluid, urine, sweat, tears, blood, serum, stool etc. However, Simonson fails to teach step (a) of the amended claim 1, which requires intermixing a PA-specific antibody and a fluorochrome tagged competitive reagent with the sample. Furthermore, Simonson does not disclose a detection method based on fluorescent polarization technique.

Response

The amended claims 1 is directed at a competitive method for detecting *Bacillus anthracis* in a sample comprising the steps: a) intermixing the sample, an antibody to protective antigen of *Bacillus anthracis*, and a competitive reagent consisting of a *Bacillus anthracis* polypeptide labeled with a

fluorochrome, which is capable of binding to that antibody, to produce a mixture; b) incubating the mixture for 15 seconds to 5 minutes; c) measuring the fluorescence polarization of the mixture, a negative control solution of the fluorochrome-labeled competitive reagent, and a positive control solution of the fluorochrome-labeled competitive reagent exposed to a known amount of protective antigen; AND d) detecting binding interaction between the protective antigen in the sample and the antibody by comparing the measured fluorescence polarization of the mixture with the measured fluorescence polarization of the negative control solution, and the positive control solution.

The examiner admits that Tencza and Nielsen do not teach using a B. anthracis polypeptide, particularly protective antigen in their assay methods. However, the examiner alleges that in view of Simonson, it would have been obvious to one of ordinary skill in the art at the time of invention that protective antigen from B. anthracis could be used in fluorescence polarization assay as outlined by Tencza or Nielsen.

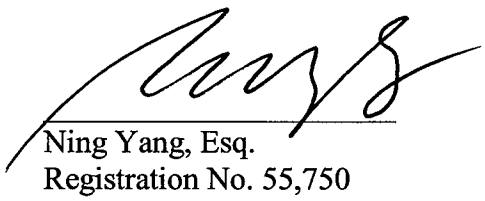
Under 35 USC §103, before answering Graham's 'content' inquiry, it must be known whether a patent or publication is in the prior art under 35 U.S.C. § 103. MPEP 2141.01(I). The applicant contends that Simonson should be removed as a prior art under 35 USC §103 (c). This application was filed on March 26, 2004, claiming priority to provisional application 60/457,940 filed March 28, 2003. Simonson was filed on January 30, 2002 and was first published on July 31, 2003. Therefore, Simonson can only qualify as a prior art under 35 USC 102(e). At the time of the invention was made, Simonson was subject to an obligation of assignment to the United States of America as represented by the Secretary of the Navy. Two assignments were later executed and recorded with the USPTO (Reel/Frame: 012780/0327, and Reel/Frame: 014011/0277). The present application is also owned by the US Navy (see attached assignments). Due to an administrative error, an incorrect recordation of assignments was filed for this application, which has been corrected. Because Simonson only qualifies as prior art under 35 USC 102(e) and the claimed invention and Simonson were, at the time the

invention was made, commonly owned by the US government, the applicants respectfully request that Simonson be removed as a prior art. Without Simonson, the combined prior art fails to teach a competitive FP detection method of B. anthracis using protective antigen.

Furthermore, Applicants contend that the combined teachings of Tencza, Nielson and Simonson fail to teach each and every element of claim 1 because the fluorescent polarization assays outlined in Tencza and Nielsen do not teach the detection of the presence of viral antigens in a sample. Instead, both references teach a method that detects the presence of a specific antibody in a sample (Tencza, Abstract, lines 8-10; Nielson, Abstract, lines 2-3; Simonson, Abstract lines 1-3). Because the assays in the prior art aim to measure antibody already existed the sample, no additional antibody need to be added to the sample. Claim 1 step (A) of the current invention, however, requires two reagents to be added to the sample including an antibody specific for B. anthracis protective antigen, and a labeled competitive reagent that binds to that antibody. Binding interactions between this added antibody and the protective antigen in the sample is then detected by competitive fluorescence polarization.

Because the combined prior art fail to teach each and every element of the current invention, the applicants respectfully request rejections against claim 1 based on 35 USC §103(a) be reconsidered and withdrawn. Furthermore, claims 2, 5-15 are dependent claims of claim 1; therefore 103(a) rejections against these claims should also be withdrawn.

Respectfully submitted,



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